

Ionic Liquid-based Sensors

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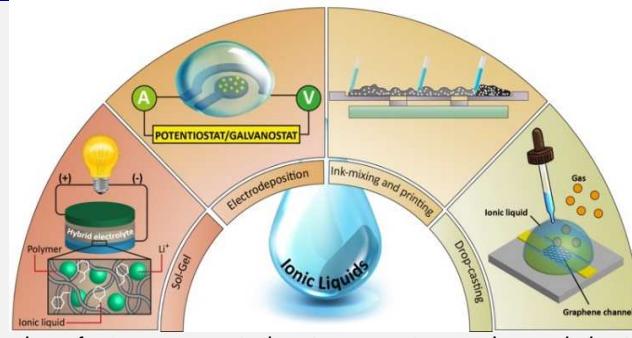


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ABSTRACT

These days Ionic liquids (ILs) are getting more attention and catching more eyes based on numerous advantages they can offer, including low volatility, excellent thermal and chemical stability, easy handling, remarkable conductivity, and facile design. These riveting materials are formed via asymmetric cations and anions. They can mainly be found in a liquid state where temperatures are below 100 °C. Therefore, due to their unique features, they can be considered a perfect and desirable candidate in several fields, including electrochemical biosensors and detecting agents; they can play their roles as electrolytes. These unique features prompted us to present a precise and short review of the different fabrication methods of Ionic liquids. Herein, after a laconic description of ILs, a diverse range of fabrication methods was investigated, and a succinct description was given in each approach. Furthermore, where needed, some clear illustrations were used to boost apprehend. Perspectives, remarks, and challenges of different fabrication methods have been given, respectively.



Keywords: Electrochemical sensors, biosensing, fabrication, ionic liquid, biomedical applications

1. Introduction

Since the dawn of the twenty-first century, there has been a growing demand for biosensors [1]. Nowadays, they can be considered one of the most thrived fields. Biochemical molecules can be employed in the biosensing process to obtain a desirable basis for selective and reliable analyses [2]. Mainly, the biosensing process can be sorted into three different groups: (i) analyte to be distinguished, (ii) signal transduction, and (iii) readout. A device with molecular sensing alongside a biological detector element can form an electrochemical biosensor with the ability to convert biological detection to a readable electrical one [3,4].

Herein, we were convinced to write a review about Ionic liquids, also known as (ILs), because they have caught our eyes for many reasons. Among them, being a prevalent organic solvent is one of the supreme ones. Conversely, Ion base nature with the liquid state at 100 °C and below temperatures give them fortés. Outstanding conductivity, negligible volatility, remarkable thermal and chemical stability, facile design, and accessibility are other advantages of these fabulous structures. On the other hand, compared to volatile organic compounds (VOCs), ILs consider more green because they do not just vanish, so they are more friendly toward the environment [5,6]. Excluding carbon dioxide and carbon monoxide, organic chemicals containing carbon that vaporize at room temperature are considered volatile organic compounds. Therefore, although Ionic Liquids were found at below 100°C, they were not vaporized

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at that temperature, which is favored for environmental application. Owning wonderful properties, it felt there was an empty place around reviewing how these riveting structures can form and fabricate. A thorough review of different fabrication methods is offered in this review. The advantage and disadvantages of these fabrication methods were discussed as well and new studies in each section were also brought with a brief explanation. Where it is needed, some riveting illustrations support the text to boost apprehension. The recent studies around each fabrication method brought in the paper and their advantages and disadvantages were subsequently given.

2. Fabrication of IL-based electrodes

Various methods have been established for fabricating IL-based electrodes. In this section, a brief description of the most widely used techniques is provided.

2.1. Direct mixing

This technique has been considerably expanded for fabricating carbon ionic liquid electrodes (CILEs). For instance, in a study, CILEs are prepared by mixing a certain amount of graphite powder with *n*-octyl pyridinium hexafluorophosphate (OPFP) in agate to fabricate a carbon composite electrode. It provided a significant increase in the rate of electron transfer of different organic and inorganic electroactive compounds and presented a noticeable decrease in the overvoltage for detecting biomolecules such as NADH, dopamine, and ascorbic acid [7,8].

In another study, a simple electrochemical sensor was designed by direct mixing of graphene nanoplatelets (GNPs) and 1-butyl-2, 3-dimethyl imidazolium tetrafluoroborate as a modifier for glassy carbon paste electrodes (GCPEs) to detect bisphenol A (BPA). The sensor provided great functionality to sense BPA in water samples in contact with plastic materials [9]. A schematic of the novel 2D heteroatom-doped carbon materials for high-performance oxygen reduction reaction (ORR) with a direct mixing method is presented in **Figure 1**.

Another example of direct mixing is entrapping materials/ biomaterials in IL-carbon paste to modify Carbone paste electrodes (CPEs) and fabricate Carbon ionic liquid paste electrodes (CILPE). For instance, a hydrophobic IL- 1-butyl-3 methyl-imidazolium hexafluorophosphate ([BMIM]PF₆) is directly mixed with a certain ratio of graphite powder and hemoglobin (Hb) to prepare a carbon paste electrode to detect acrylamide (AA). Compared with other electrochemical methods for detecting AA, the electrochemical biosensor demonstrated various advantages such as simple preparation, easy surface renewal, better reproducibility, and excellent stability [10].

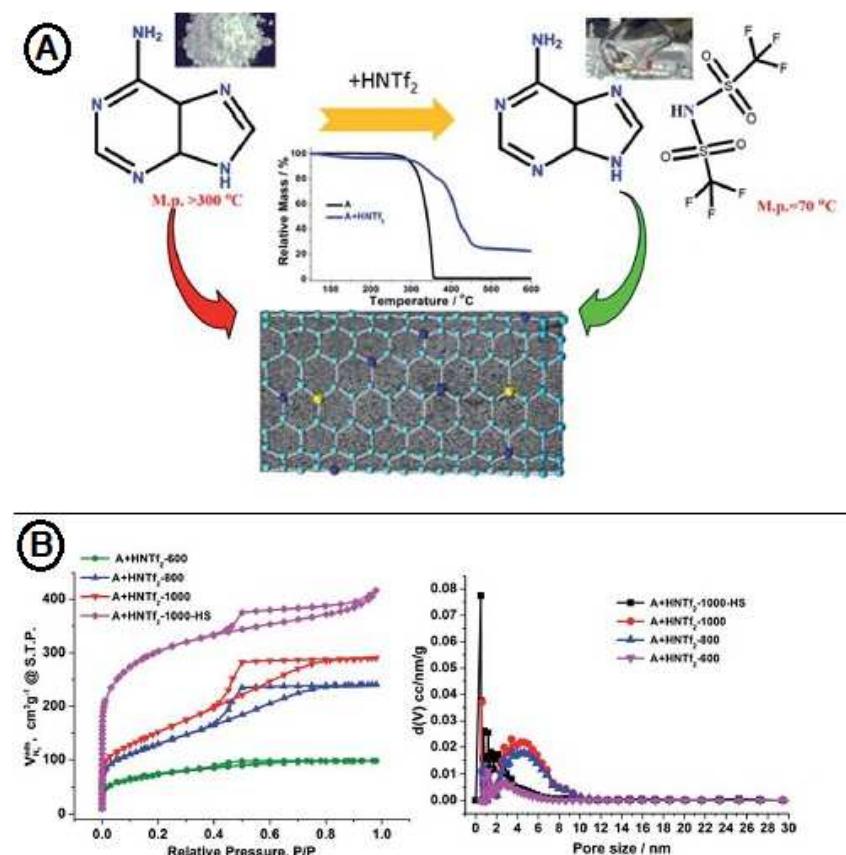


Figure 1. (A) The synthetic routine of adenine-based ILs for doped carbon synthesis with direct mixing method, (B) N₂ sorption isotherm of the ion thermal carbons derived from adenine-based ionic liquids and pore size distribution of related adenine based ionic liquids. Reprinted with permission from [9].

2.2. Casting and rubbing

Casting is a manufacturing process in which liquid materials are generally poured into a mold. This method is used to create protein-based biosensors by stabilizing biomolecules onto carbon nanotube (CNT)/IL-nanocomposite-modified films [11]. As can be seen in **Figure 2**, a schematic of the casting method brought in which sulfonated poly(ether ether ketone) doped with ammonium Ionic Liquids and nano-silicon dioxide for polymer electrolyte membranes fabrication.

In the rubbing method, by grinding a certain amount of premixed biomolecule/CNTs with an Ionic Liquid, a dark gel would be formed that can be coated on a glass side. This treated glassy carbon electrode can be mechanically rubbed to and would attach the gel to the surface. For instance, protein-based biosensors are mainly manufactured by this method (through stabilization of biomolecules onto carbon nanotube (CNT)/IL-nanocomposite-modified films).

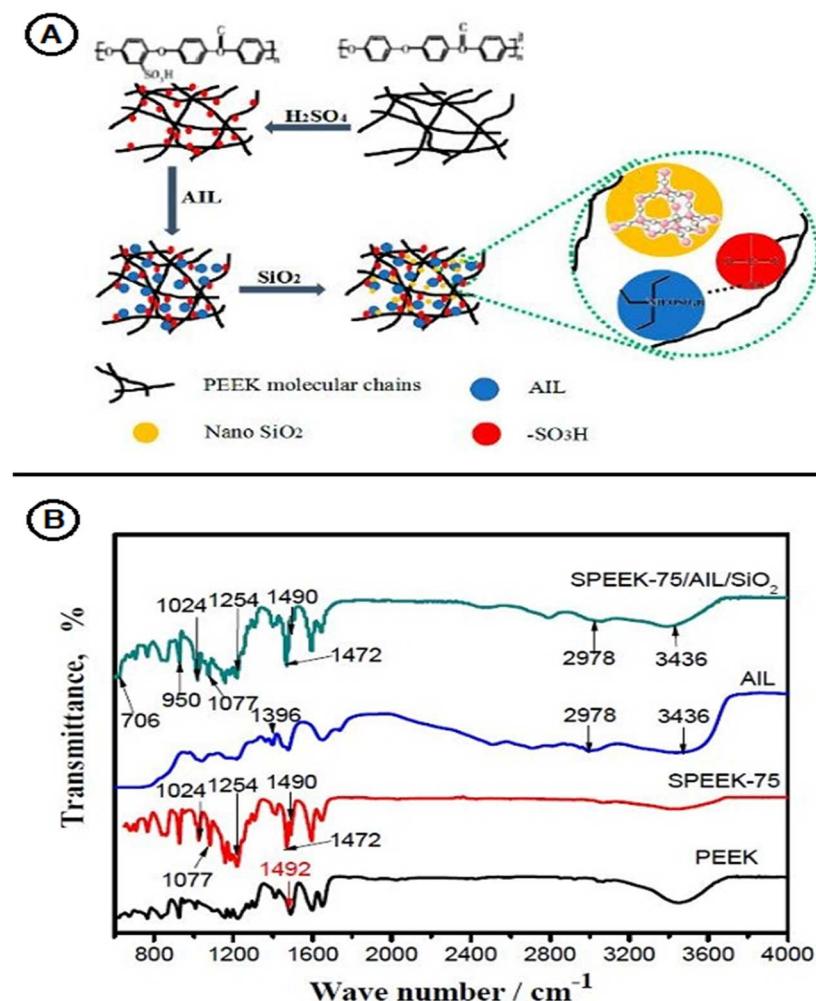


Figure 2. (A) Schematic representation of the ternary composite membrane preparation process via casting approach (B) The Fourier transform infrared (FTIR) spectra of the poly(ether ether ketone) (PEEK), sulfonated poly(ether ether ketone) (SPEEK)-75, AIL, and SPEEK-75/AiL/SiO₂ composite membranes. Reprinted with permission from [12].

2.3. Physical adsorption

This method is based on nonspecific physical adsorption between the surface of the support electrode and proteins using ionic forces. The nature of the forces can be reversed by altering the conditions that influence ionic strength. Physical absorption is a low-cost but challenging method. For instance, one of the common problems in this method is enzyme leakage from the matrix and the relatively weak interactions. However, using Ionic liquids as an alternative can exclude these problems and improve biosensor performance [13].

2.4. Electrodeposition

The electrodeposition method is defined as a film development procedure that lies on the foundation of a metallic cladding on a substrate by electrochemical reduction of metal ions from an electrolyte. This method aims to achieve promising electrical and corrosion resistance, better heat tolerance, and improved heat resistance. According to their characteristics, naming nonflammability, negligible vapor pressure, and heat resistant nature, ionic liquid materials are a suitable medium for the electrodeposition of metals and semiconductors [14].

Diminishing electrodeposition of metals has been impossible in an aqueous solution; however, the use of Ionic Liquids makes this impossible, possible and obtains the redox chemistry, and controls the metal nucleation characteristics [15].

2.5. Layer-by-layer method

Among different techniques used for the immobilization of enzymes, the layer-by-layer (LBL) method has attracted much attention due to its simple process and accurate control of film composition, thickness, roughness, and porosity. In addition, using this method, various materials can be used in the fabrication of films [16–19]. Therefore, the layer-by-layer technique has established significant attention in the field of electrochemistry as a capable tool for the fabrication of nanostructured films and their application in sensors and biosensors [20,21]. This method adsorbs electrolytes and enzymes from solution onto an electrode surface through electrostatic adsorption or covalent bond formation [22,23].

In the layer-by-layer method, Ionic Liquids can be used not only as the supporting electrolyte but as the modifier in the chemically modified electrodes [24–26]. In addition, the nanocomposites containing Ionic Liquids and different nanomaterials such as gold nanoparticles [27–30], Titanium Nitride (TiN) [31–34], TiO₂-graphene nanocomposites [35–38], and CNTs-gold nanoparticles [39–41] have been utilized for fabricating the third generation of biosensors.

For example, a layer-by-layer approach is used for fabricating a biosensor consisting of glassy carbon (GC) electrode modified by a multilayer of catalase and nanocomposite containing 1-(3-Aminopropyl)-3-methylimidazolium bromide (amine-terminated ionic liquid (NH₂-IL)) and titanium nitride nanoparticles (TiNnp). This biosensor demonstrated good stability, high reproducibility, long lifetime, and fast amperometric response. In addition, a high sensitivity ($380 \text{ A mM}^{-1} \text{ cm}^{-2}$) and low detection limit (100 nM) at a concentration range up to 2.1 mM have been achieved [42].

In one fascinating article, foams with high porosity and low rigidity fabricated which integrated with ionic liquid (IL), achieve super high sensitivity up to $9,280 \text{ kPa}^{-1}$. An open-cell polyurethane (PU) foam with a porosity higher than 98.8% was selected to serve as the 3D skeleton, then loading IL on the pore walls to create a continuous ionic layer. The PU-IL composite exhibits an extremely low engineering modulus ($\sim 3.4 \text{ kPa}$) due to the high porosity and offers minimized initial contact area between the electrode and the ionic layer (**Figure 3**) [43].

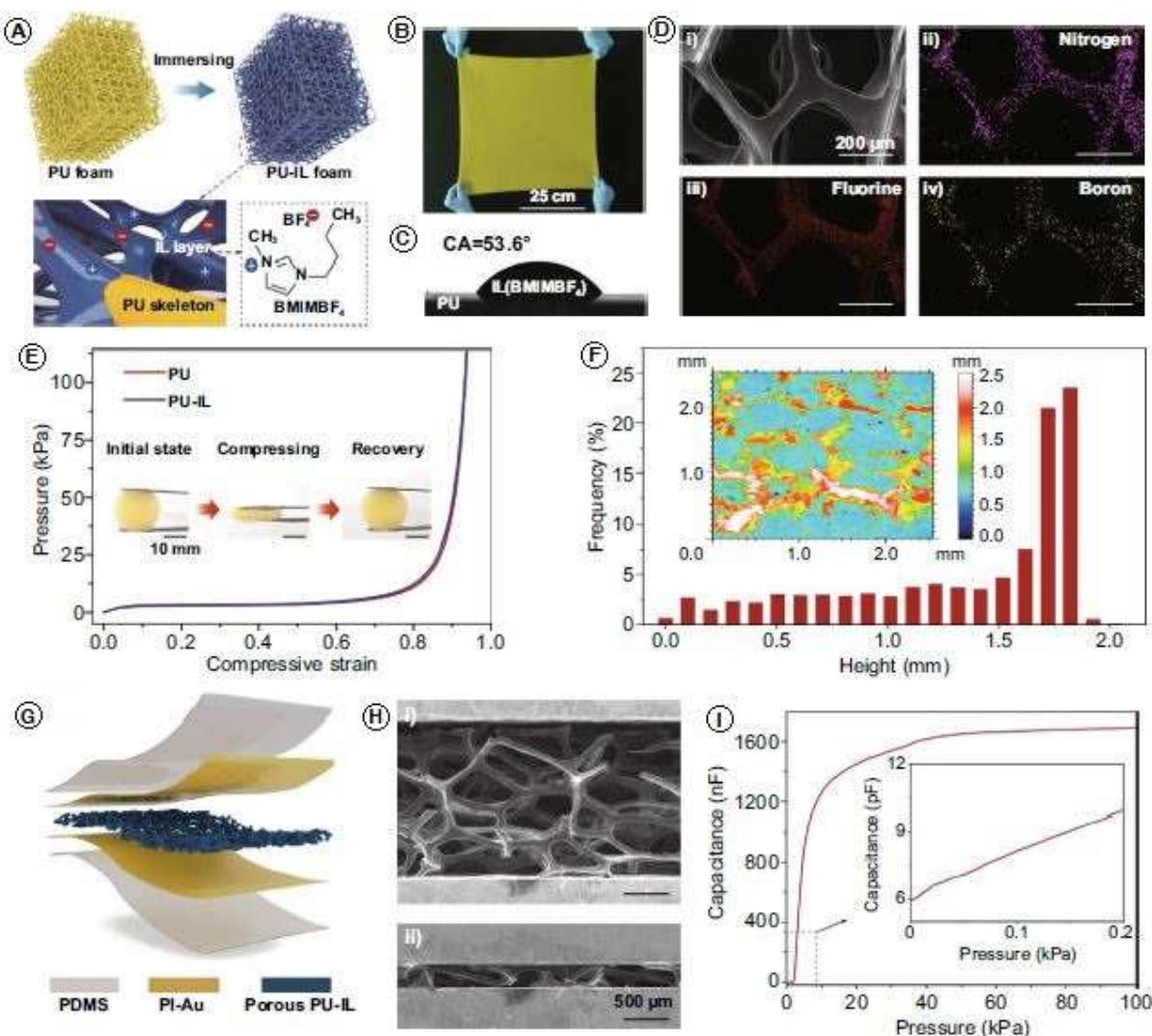


Figure 3. PU-IL composite foam, flexible capacitive-type pressure sensor, and its sensing property. **(A)** Schematic of a PU-IL composite foam with IL on the surface of PU skeleton. **(B)** A PU-IL composite foam with a dimension of 50 cm × 50 cm × 2 mm. **(C)** Contact angle of IL on the surface of PU plate. **(D)** Elemental mapping of nitrogen, fluorine, and boron of the PU-IL composite foam. **(E)** Stress-strain curves of PU and PU-IL composite foams under compression. **(F)** Height distribution of the PU-IL composite foam. **(G)** Schematic of a capacitive-type pressure sensor that consists of two PI-Au electrodes, a PU-IL composite foam, and a PDMS sealing layer. **(H)** SEM images of the PU-IL foam before and after compression. **(I)** Capacitance as a function of the pressure of the sensor using our PU-IL composite foam. Reprinted with permission from [43].

2.6. Sol-gel encapsulation

A key characteristic for the application and development of biosensors is a biocompatible and constant matrix for immobilizing the enzyme [44]. The sol-gel matrix material has exceptional properties of physical stiffness, chemical lifelessness, photochemical strength, thermal stability, and negligible swelling in aqueous and carbon-based solvents [45].

Therefore, the sol-gel encapsulation method is exceptionally eye-catching for the fabrication of biosensors [46]. On the other hand, Ionic Liquids have also been widely used in biocatalysis for their outstanding biocompatibility and it has been demonstrated that enzymes of various types can provide their activities in Ionic Liquids or aqueous biphasic Ionic Liquid systems. In addition, the Ionic Liquids increased the reusability and steadiness of the enzymes. Consequently, many studies have applied Ionic Liquids in a sol-gel matrix for the detection of different analytes. For instance, a horseradish peroxidase (HRP)-immobilized room temperature Ionic Liquid-based sol-gel matrix for the

preparation of an electrochemical amperometric biosensor has been reported. It is also established that the viscous Ionic Liquid prevented the cracking of the sol-gel-derived glasses. The Ionic Liquids–gel enzyme electrodes preserved the high activity of HRP and provided long-lasting permanency of HRP in storage. This biosensor provided a favorable platform for the development of affinity supports and biosensors as well as in the application of ILs [47].

There is a report about silica microcapsules containing phosphonium ionic liquid (IL), denoted $\text{SiO}_2@\text{IL}$, successfully synthesized for the first time using the one-step sol-gel method in $\text{IL}/\text{H}_2\text{O}$ emulsion. This work was dedicated to the encapsulation of phosphonium ionic liquids in a silica shell or IL microcapsules as a functional additive in epoxy networks. Thus, inspired by self-healing IL-epoxy composites and encapsulation of IL, and aims to design through a simple route a new type of phosphonium ionic liquid core/silica shell microcapsule prepared using sol-gel chemistry in microemulsion, in which a silica shell provides the perfect stability of the IL until the breakage of the microcapsules (**Figure 4**) [48].

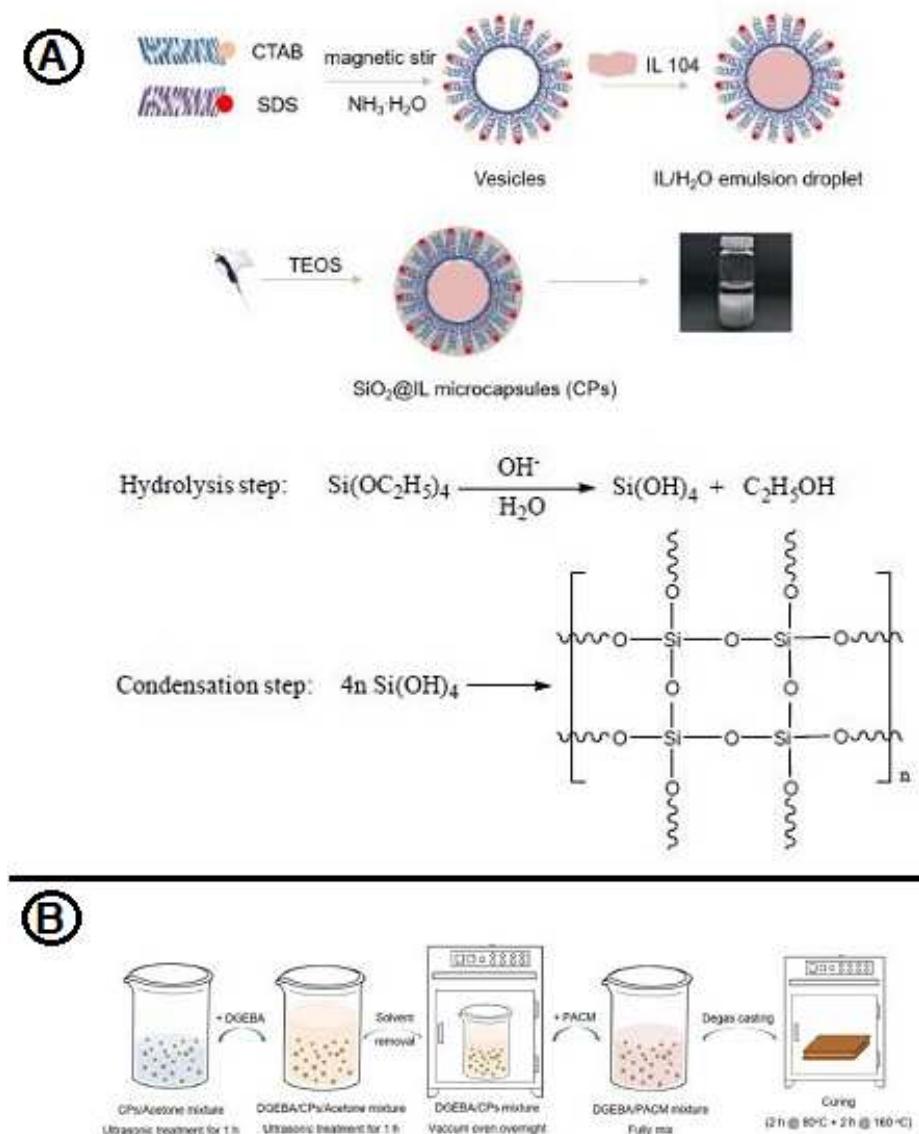


Figure 4. (A) Different steps of the synthesis of silica microcapsule containing phosphonium Ionic Liquid ($\text{SiO}_2@\text{IL}$). (B) The schematic preparation procedure of $\text{SiO}_2@\text{IL}$ CPs/epoxy-amine networks. Reprinted with permission from [48].

2.7. Sandwich-type immunoassay

A sandwich-type approach consists of restricting the target antigen on the surface of the carbon ionic liquid electrodes, between antibody and secondary antibody marked with horseradish peroxidase (HRP) [49]. HRP catalyzes H_2O_2 and therefore the reaction between O-aminophenol and H_2O_2 generates a voltammetric signal, which is directly proportional to the concentration of the target antigen attached to the sensing layer as **Figure 5** brought illustrates the localized and delocalized process in the Ar matrix and ionic liquid glass upon radiolysis and further annealing [50,51].

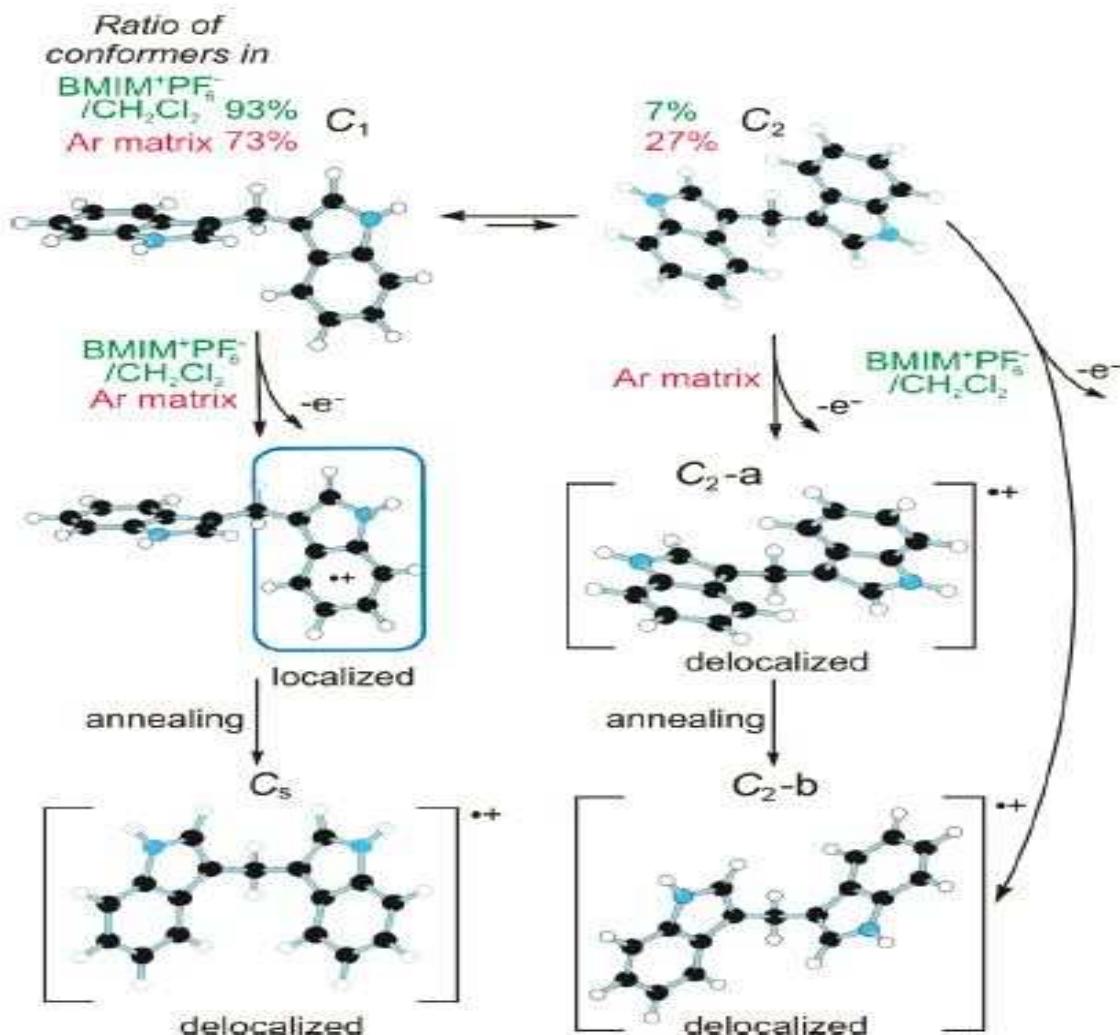


Figure 5. Two separate processes occur in Ar matrix and ionic liquid glass upon radiolysis and further annealing. Reprinted with permission from [52].

In sandwich-type strategy, signal amplification and noise reduction are notable. Consequently, ILs were effectively used in this method to provide a convenient pathway and electrode surface. In addition, I perform a fundamental role in increasing the sensitivity of the immunosensor when used in the structure of a carbon-based electrode [53,54]

2.8. Screen-printed ionic liquid/graphene-based electrochemical sensors

Screen printing is one of the practical processes that can meet most fabrication requirements, such as productively and reproducibly at a low cost for industrial use. Accordingly, screen-printed electrodes (SPEs) have been widely used in electrochemical analyses [55–59].

Although there is no study indicating a direct fabrication of electrodes using inks containing Ionic Liquids and graphene (GP), there are studies that employed screen printing by using mixtures of ILs and graphene to fabricate superior electrodes in terms of uniformity, reusability, and controllability when compare with IL-modified SPEs [60]. **Figure 6** portraits a screen-printed ionic liquid-graphene electrode using 3-methyl-1-propylpyridinium bis(trifluoromethyl sulfonyl)imide (PMPIm), carbon paste, and graphene.

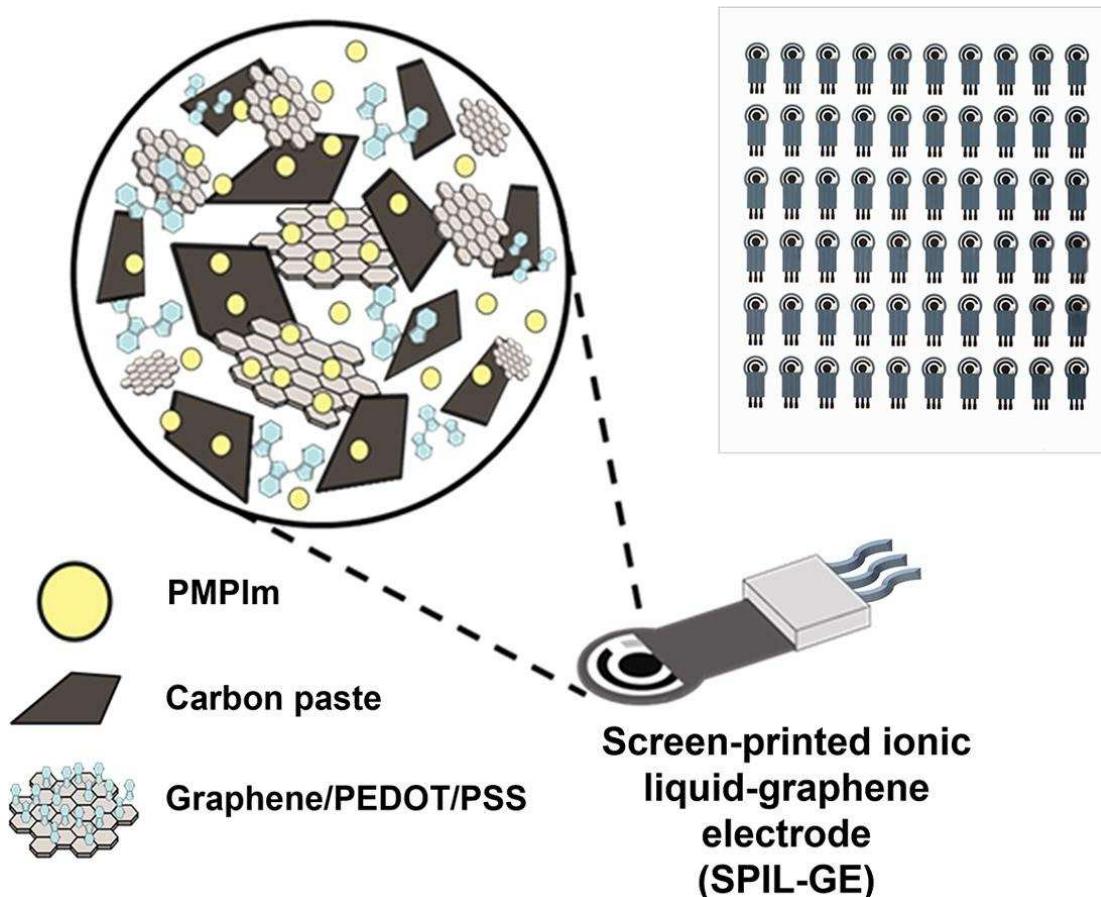


Figure 6. Screen-printed ionic liquid-graphene electrode using 3-methyl-1-propylpyridinium bis(trifluoromethyl sulfonyl) imide (PMPIm), carbon paste, and graphene. Reprinted by permission from [60].

3. Conclusion

A diverse range of methods to fabricate IL-based electrodes was investigated in this paper. One of the most striking fillers recently developed is Ionic liquids (ILs). These emerging structures were formed in different ways, eight ways investigated in this review, and their advantages and disadvantages were scrutinized systematically. Recent papers on each method were brought. Where the direct mixing method is favorable for electrochemical biosensors, the rubbing method is used to create protein-based biosensors.

Although physical adsorption and electrodeposition methods suffer from leakage and impossible redox in an aqueous solution, the Ionic liquids help them overcome those features. In the layer-by-layer method, Ionic liquid played as a supporting electrolyte and modifier, which is favorable. The Ionic Liquid sol-gel enzyme electrodes not only preserved the high activity of horseradish peroxidase but also led to more long-term permeance of HPR. In addition, Ionic liquids play a vital role in augmenting the sensitivity of the sandwich-type immunosensors. Uniformity, reusability, and controllability are the merits of using modified Ionic Liquid in the screen-printing sensors. Conversely, ILs have been used for biomaterials applications, too.

However, there is a long way ahead. In the future, ILs can be used in the preparation, improvement, dissolution, and processability, and can be combined with natural and synthetic polymer matrixes to develop IL-polymer hybrid materials to be employed in different fields of the biomedical area. Overall, this review revealed that using Ionic liquid can enhance each method's performance in different ways.

Authors' contributions

All authors contributed to drafting and revising of the paper and agreed to be responsible for all the aspects of this work.

Declaration of competing interest

The authors declare no competing interest.

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Data availability

Not applicable.

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